UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,532	10/06/2003	Nicholas M. Dean	ISPH-0782	3966

7590 01/14/2005

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, NJ 08053

EXAMINER	
CHONG, KIMBERLY	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 01/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/679,532	DEAN ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 73-97 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 73-97 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12/17/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claim 97, drawn to a composition comprising an antisense oligonucleotide targeted to interleukin-5, classifiable in class 536, subclass 24.5.

II. Claims 73-96, drawn to methods of inhibiting expression of interleukin-5, and to methods of treating an individual comprising the use of antisense compounds targeted to interleukin-5, classifiable in class 514, subclass 44.

The inventions are distinct, each from the other because of the following reasons:

Inventions of group I and group II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product antisense oligonucleotides of group I can be used as probes for identifying the presence of specific mRNA transcripts in *in situ* hybridization assays, which does not involve administering antisense oligonucleotides to cells or tissues of individuals, as present in group II.

During a telephone conversation with Jane Licata on 12/07/04 a provisional election was made with traverse to prosecute the invention of group II, claims 73-96. Affirmation of this election must be made by applicant in replying to this Office action. Claim 97 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 73-76 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Nyce et al. (WO 96/40162).

Claims 73-76 and 78 are drawn to methods of inhibiting expression of interleukin-5 in cells or tissues by administration of a modified antisense compound targeted to interleukin-5.

Nyce et al. discloses antisense compounds targeted to interleukin-5 (see page 31, lines 5-10). Nyce et al. further discloses modification of antisense compounds (see pg 8, lines 28-37 and page 9, lines 1-30) and methods of inhibiting interleukin-5 in cells or tissues by administration of an antisense compound targeted to interleukin-5 (see claims 1 and 5).

Claims 73-76 and 78 are rejected under 35 U.S.C. 102(e) as being anticipated by Nyce et al. (WO 99/13886).

Claims 73-76 and 78 are drawn to methods of inhibiting expression of interleukin-5 in cells or tissues by administration of an antisense compound targeted to interleukin-5 and further where the antisense compound if modified.

Nyce et al. discloses antisense compounds targeted to interleukin-5 (see page 49). Nyce et al. further discloses modification of antisense compounds (see pg 15, lines 10-35) and methods of inhibiting interleukin-5 in cells or tissues by administration of an antisense compound targeted to interleukin-5 (see claims 2, 9 and 52).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 77 and 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nyce et al. (WO 96/40162) in view of Barracchini et al. (U.S. Patent Number 5,801,154).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The invention of the above claims is drawn to a method of inhibiting expression of interleukin-5 in cells or tissues comprising contacting cells or tissues with an antisense compound and further where said antisense compound comprises sugar and base modifications.

Nyce et al. teach methods of inhibiting interleukin-5 in cells or tissues by administration of an antisense compound targeted to interleukin-5 and further disclose

modifications of antisense compounds. Nyce et al does not teach modified antisense compounds comprising 2'-MOE sugar modifications nor 5-me pyrimidine modifications such as 5-methyl cytidine.

Baracchini et al. teach modifications of antisense compounds comprising 2'-MOE sugar modifications and 5-me pyrimidine modifications, including 5-me cytosine (see column 7, lines 20-25).

It would have been obvious for one of ordinary skill in the art to incorporate the oligonucleotide modifications of Baracchini et al. into the already modified antisense oligonucleotides targeting interleukin-5 as taught by Nyce et al. One would have been motivated to create such modified compounds because Nyce et al. expressly teach that the modified antisense oligonucleotides are more stable and allow for increased cellular permeation, and because Baracchini et al. teach a number of modifications, such as sugar modifications and base modifications, including 5-methyl cytosine, that serve to increase an antisense compound's cellular uptake, target affinity and resistance to degradation. Therefore, one of ordinary skill would have been motivated to use other types of modifications that confer the same advantages of increased cellular uptake and resistance to degradation, such as those taught by Baracchini et al.

Finally, one would have a reasonable expectation of success given that Baracchini et al. teach all the steps necessary to make such modified antisense compounds including starting reagents, concentrations, and incubation times, the steps of which are routine to one of ordinary skill in the art.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 79, 84-86 and 94-95 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 79 recites the limitation "said base modification". There is insufficient antecedent basis for this limitation in the claim.

Claim 84 recites the limitation "said sugar modification". There is insufficient antecedent basis for this limitation in the claim.

Claim 85 recites the limitation "said internucleoside modification". There is insufficient antecedent basis for this limitation in the claim.

Claim 86 recites the limitation "said base modification". There is insufficient antecedent basis for this limitation in the claim.

Claims 94 and 95 recite the limitation "said oligonucleotide". There is insufficient antecedent basis for this limitation in the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 73-96 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 73 is drawn to a method of inhibiting expression of interleukin-5 in cells or tissues using an antisense compound targeted to interleukin-5. Claims 74-79 limit claim 73 by stating the modifications of the antisense compound. Claim 80 is drawn to a method of reducing eosinophilia in an individual comprising administering an antisense compound targeted to interleukin-5. Claims 81-86 limit claim 80 by stating the modifications of the antisense compound. Claim 87 is drawn to a method of treating airway hyperresponsiveness or pulmonary inflammation in an individual comprising administering an antisense compound targeted to interleukin-5. Claims 88-93 limit claim 87 by stating the modifications of the antisense compound. Claim 94, 95 and 96 further limit claim 87 by stating the antisense compound is aerosolized and inhaled, the antisense compound is administered intranasally, intrapulmonarily or intratracheally,

and the airway hyperresponsiveness or pulmonary inflammation is associated with asthma, respectively.

Example 10 of the specification teaches 25 antisense compounds targeted to one variant of murine interleukin-5. Example 20 of the specification teaches antisense sequence compounds targeted to one variant of human interleukin-5. However, the claims are broadly drawn to methods of inhibiting using antisense targeted to any interleukin-5 gene from any species. Although the specification as filed describes antisense compounds targeted to murine interleukin-5, this does not provide a description for other species because the species is highly variant. Further, the specification as filed does not describe, by structure (i.e. nucleotide sequence), antisense to the many different species of interleukin-5 genes as necessary to allow one skilled in the art to envisage a sufficient number of species of antisense required for the claimed genus of antisense needed to practice the genus of methods of inhibition of expression of interleukin-5 and methods of treating a disease associated with the expression of interleukin-5, encompassed in the claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

MPEP 2163 states in part, "An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.")

Thus, the instantly claimed invention cannot be said to have been adequately described in a way that would convey with reasonable clarity to those skilled in the art that, as of the filling date sought, applicant was in possession of the claimed invention because the specification, while providing information on antisense compounds targeted to murine interleukin-5 mRNA, does not provide any other information or guidance as to what antisense sequence for any nucleic acid encoding interleukin-5 from any other species and further provide treatment or prevention of airway hyperresponsiveness or pulmonary inflammation.

Claims 73-96 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of interleukin-5 *in vitro* using antisense compounds and enabling for reduced levels of esophinilia in a mouse inflicted with airway inflammation after administration of an antisense compound targeted to interleukin-5, does not reasonably provide enablement for prevention of airway hyperresponsiveness or pulmonary inflammation by administration of an antisense compound, intranasally, intrapulmonarily or intratracheally targeted to interleukin-5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims

The instant claims are drawn to an antisense compound targeted to interleukin-5 in cells or tissues and to a method of reducing eosinophilia in an individual comprising administering an antisense compound targeted to interleukin-5. Further, the instant claims are drawn to a method of treating airway hyperresponsiveness or pulmonary inflammation in an individual comprising administering an antisense compound targeted to interleukin-5.

The specification as filed teaches inhibition of murine interleukin-5 *in vitro* by administration of an antisense targeted to a nucleic acid gene encoding interleukin-5 (see example 10 of the specification). The specification as filed teaches the effect of administration of an antisense compound targeted to interleukin-5 on the eosoniphil infiltration in the airway of an ovalbumin-induced hyperresponsiveness of a mouse (see example 18 of the specification). Further, the specification as filed teaches the inhibition

of human interleukin-5 in vitro by administration of an antisense targeted to a nucleic acid gene encoding interleukin-5 (see example 20 of the specification). The specification as filed does not teach that because of administration of an antisense compound targeted to interleukin-5, interleukin-5 is inhibited, eosinophil specific inflammation is prevented and therefore provide treatment of conditions and diseases associated with eosinophilic inflammation *in vivo*.

There is no guidance in the specification as filed that teaches how to target the claimed antisense compound to human cells or tissues, inhibit the expression of interleukin-5 *in vivo*, and further provide treatment for hyperresponsiveness or pulmonary inflammation. Although the specification discloses inhibition of human interleukin-5 mRNA *in vitro* by administration of antisense compound, such a disclosure would not be considered enabling since the state of antisense-mediated gene inhibition is highly unpredictable.

The following factors have been considered in the analysis of enablement: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples, (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claimed breadth of claims 73-96 encompass methods of treating a broad range of diseases in different tissues by use of an antisense targeted to interleukin-5 gene *in vivo*. Although the specification teaches inhibition of human interleukin-5

mRNA *in vitro* after treatment with an antisense compound (see example 20), this guidance is not sufficient to resolve the known unpredictability in the art associated with appropriate *in vivo* delivery and treatment effects provided by the instantly claimed methods.

The references cited herein illustrate the state of the art for therapeutic *in vivo* applications using antisense compounds. Branch stresses that "because it is very difficult to predict what portions of an RNA molecule will be accessible in vivo, effective antisense molecules must be found empirically by screening a large number of candidates for their ability to act inside cells" (TIB 23: 45-50 1998). Green *et al.* states that "[i]t is clear from the evolution of antisense technology from a laboratory research tool into a mechanism for designing active and effective drugs is far from complete. Although there is little doubt that systemically administered antisense [oligonucleotides] can inhibit the expression of specific genes in patients, the effectiveness of such therapy in modifying the course of a particular illness has not yet been established. In addition, toxicity in humans appears more problematic than might be predicted based on preclinical studies in rodents. Clearly, additional work must be done to unravel the complex problems associated with drug delivery, mRNA targeting and aptameric, nonantisense effects" (Antisense Therapy in Human Disease; Vol. 191, No. 1 2000, pg 103 column 2).

The problems with efficient delivery of antisense oligonucleotides to cells has been addressed by Jen *et al.*, who states that "[o]ne of the major limitations for the therapeutic use of AS-ODNS ...is the problem of delivery....presently, some success

has been achieved in tissue culture, but efficient delivery for *in vivo* animal studies remains questionable (Stem Cells 2000; 18:307-319 pg 315 column 2)." Jen *et al.* concludes that "[g]iven the state of the art, it is perhaps not surprising that effective and efficient clinical translation of the antisense strategy has proven elusive (see p 315, second column)."

As outlined above, it is well known that there is a high level of unpredictability in the antisense art for therapeutic *in vivo* applications. The scope of the claims in view of the specification as filed together do not reconcile the unpredictability in the art to enable one of skill in the art to make and/or use the claimed invention, namely treatment of airway hyperresponsiveness or pulmonary inflammation by administration of an antisense compound targeted to a gene encoding interleukin-5.

While one skilled in the art may be able to find an antisense oligonucleotide targeted to a gene encoding interleukin-5 and demonstrate inhibition of interleukin-5 in cells *in vitro* after treatment with the antisense oligonucleotide, the specification as filed does not teach how to administer any antisense oligonucleotide to airway hyperresponsiveness or pulmonary inflammation and further to treat by administration of the antisense compound intranasally, intrapulmonarily or intratracheally, as claimed. Crooke (Antisense Research and Application; Chapter 1, Springer-Verlag, New York. 1998) supports the difficulties of extrapolating from in vitro experiments and states on p. 3, paragraph 2, "extrapolations from *in vitro* uptake studies to predictions about *in vivo* pharmacokinetic behavior are entirely inappropriate and, in fact, there are now several lines of evidence in animals and man [that] demonstrate that, even after careful

consideration of all *in vitro* uptake data, one cannot predict *in vivo* pharmacokinetics of the compounds based on *in vitro* studies [references omitted]."

Furthermore, although the specification discloses a murine model of allergic asthma and discloses that because of administration of an antisense compound to a mouse, treatment of airway hyperresponsiveness or pulmonary inflammation associated with asthma was provided. Such a disclosure would not be considered enabling because the murine model of allergic asthma is not considered an accurate representation of human asthma pathology.

The art-accepted animal model of human asthma has some limitations as noted by Richards, I.M. (Clinical and Experimental Allergy, 1996 Vol. 26:618-620) who states that "all animal models of bronchopulmonary eosinophilia are not equal, and none of these are asthma....[M]urine models of antigen-induced lung eosinophilic inflammation have been developed which have many features in common with asthma, but as far as we know, none of these demonstrate an inflammatory pathology which is similar to that seen in the disease in man (see page 619. last paragraph). Humbert et al. (Am. J. Respir. Crit. Care Med., 1997 Vol. 156:704-708) emphasizes more of the limitations of the animal model of asthma and states that the problems of the animal models of asthma are that "since the precise mechanism of bronchial hyperreactivity in human asthma is unknown, it is difficult to assume that experimental manipulations that produce bronchial hyperreactivity in animals, although arguable physiologically similar to that observed in humans, are also pathogenetically similar (see pg. 709, last

paragraph). Temelkovski et al. (Thorax 1998 53:849-856) asserts that the animal models of asthma "do not usually exhibit the mucosal inflammation and recruitment of eosinophils into the epithelial layer that are characteristically associated with human asthma...[and] the majority involve relatively short exposure to aerosolized antigen... and are thus devoid of the chronic inflammatory and epithelial changes that typify human asthma (see page 850, column 1)." Kumar et al. (Immunology and Cell Biology 2001 Vol. 79:141-144) agrees with Temelkovisi et al. by stating that the animal models of asthma "fail to exhibit characteristic features of human asthma...[T]he airways of mice have different structure and branching pattern compared to humans, their respiratory rate is much higher and their tidal volume is relatively small. Although these issues are often ignored by investigators, they probably account for the absence of 'clinical' manifestations in all murine models of asthma (see page 141, column 1 and page 143, column 1)".

In view of the unpredictability in the art of antisense-based therapy, as outlined above, and the unpredictability of applicant's animal model of human asthma, the specification as filed does not provide adequate guidance that would show how one skilled in the art would practice the claimed invention without undue experimentation.

Given the teachings of the specification as discussed above, one skilled in the art would not know *a priori* whether introduction of antisense oligonucleotides *in vivo* by the broadly disclosed methodologies of the instantly claimed invention, would result in successful inhibition of expression of a target gene. To practice the claimed invention, one of skill in the art would have to *de novo* determine; the stability of the antisense

molecule *in vivo*, delivery of the antisense molecule to the whole organism, specificity to the target tissue *in vivo*, dosage and toxicity *in vivo*, and entry of the molecule into the cell *in vivo* and the effective action therein. Without further guidance, one of skill in the art would have to practice a substantial amount of trial and error experimentation, an amount considered undue and not routine, to practice the instantly claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 73-86 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26 and 27 of U.S. Patent No. 6,136,603. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed method of inhibiting the expression of interleukin-5 in cells or tissues by administration of an antisense compound targeted to interleukin-5 would fully embrace the methods of inhibiting the

expression of interleukin-5 in cells or tissues *in vitro* by administration of an antisense compound targeted to interleukin-5 of U.S. Patent No. 6,136,603.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached at 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It

also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Kimberly Chong
Examiner
Art Unit 1635

KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER